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Supplementary Table 1. Population and design of each contributed study

Cancer	Study	Locations	Design
Initial analytical data in GAME-ON			
Colon & Rectum (CORECT)	MECC	US	Cohort
	CFR	US	Cohort
	Kentucky	US	Pop. CC
	CPS-II/ACS	US	Cohort
	Melbourne	Australia	Cohort
	Newfoundland	Canada	Pop. CC
Lung (TRICL)	MDACC	US	Hospital CC
	ICR	UK	Hospital CC
	Toronto	Canada	Clinic CC
	IARC	Europe	Hospital CC
	GLC	German	Pop. CC
	NCI	US	Pop. CC and nested CC
Ovary (FOCI)	UKGWAS	UK	CC
	USGWAS	US, Canada, Poland	CC
	U19	US	CC
Prostate (ELLIPSE)	BPC3	US	CC, nested CC
	CRUK1	UK	CC
	CRUK2	UK	CC
	CAPS1	Sweden	CC
	CAPS2	Sweden	CC
Replication data			
Prostate (PLCO)	PLCO	US	Nested CC
Colon & Rectum			

(GECCO)	ASTERISK	France	Hospital CC
	COLO23	US	Pop. CC
	DACHS1	Germany	Pop. CC
	DACHS2	Germany	Pop. CC
	DALS1	US	Pop. CC
	DALS2	US	Pop. CC
	HPFS1	US	Nested CC
	HPFS2	US	Nested CC
	HPFSad	US	Nested CC
	MEC	US	Nested CC
	NHS1	US	Nested CC
	NHS2	US	Nested CC
	NHSad	US	Nested CC
	OFCCR	Canada	Pop.CC
	PHS1P2	US	Nested CC
	PLCO1	US	Nested CC
	PLCO2	US	Nested CC
	PMH	US	Pop. CC
	VITAL	US	Nested CC
	WHI1	US	Nested CC
	WHI2	US	Nested CC

CC: case-control

Supplementary table 2. Gene- and pathway-based p-values for overall and aggressive prostate cancer

Gene	Chr	Combined results (14818 cases, 14227 controls)		Aggressive prostate (up to 4446 cases, 12724 controls)	
		N.SNPs	P-value	N.SNPs	P-value
Circadian rhythm pathway					
ARNTL	11	80	0.29	80	0.54
CK1E	22	48	0.30	48	0.58
CLOCK	4	24	0.021	24	0.093
CRY1	12	35	0.55	35	0.87
CRY2	11	20	0.043	20	0.57
NPAS2	2	167	0.0062	167	0.18
PER1	17	30	0.063	30	0.70
PER2	2	50	0.060	50	0.23
PER3	1	67	0.24	67	0.030
Pathway-level		521	0.0016*	521	0.29
Melanotin pathway					
AANAT	17	38	0.00078*	38	0.47
DDC	7	84	0.050	84	0.49
MTNR1A	4	35	0.35	35	0.22
MTNR1B	11	23	0.96	23	0.32
TPH1	11	18	0.15	18	0.96
TPH2	12	65	0.21	65	0.35
Pathway-level		263	0.0060*	263	0.66

*Statistically significant after Bonferroni correction ($p < 0.05/8=0.00625$ at pathway level; $p < 0.05/60=0.00083$ at gene level)

P<0.05 in bold

Supplementary Table 3. Comparison of SNP-based results between overall and aggressive prostate cancer*

Gene	SNP*	Allele		log(OR)	Overall		Aggressive		
		Ref**	Eff**		SE	P-value	log(OR)	SE	P-value
Circadian rhythm pathway									
CLOCK	rs62309758	T	C	-0.09	0.03	1.45E-03	-0.09	0.04	7.57E-03
CRY2	rs7108730	T	C	0.08	0.03	3.66E-03	0.06	0.04	1.05E-01
NPAS2	rs2305160	A	G	0.08	0.02	3.47E-05	0.06	0.03	3.00E-02
Melatonin pathway									
AANAT	rs150316415	G	A	0.28	0.07	3.41E-05	0.16	0.08	6.49E-02
DDC	rs12718611	G	A	-0.11	0.04	1.72E-03	-0.07	0.05	1.12E-01

*SNPs with the smallest p-value in the genes with $P_{\text{gene}} \leq 0.05$, based on association with overall prostate cancer.

**reference and effect alleles

Supplementary table 4. Gene- and pathway-based p-values for colorectal cancer in GAME-ON and replication samples

Gene	Chr	Game-ON (CORECT) (5100 cases, 4831 controls)		GECCO (10738 cases, 13328 controls)		Combined results (15838 cases, 18159 controls)	
		N.SNPs	P-value	N.SNPs	P-value	N.SNPs	P-value
Circadian rhythm pathway							
ARNTL	11	114	0.0044	113	0.78	140	0.028
CK1E	22	38	0.14	55	0.18	68	0.24
CLOCK	4	47	0.18	35	0.34	53	0.11
CRYI	12	56	0.81	47	0.83	73	0.95
CRY2	11	35	0.64	32	0.85	41	0.91
NPAS2	2	202	0.011	212	0.82	245	0.51
PER1	17	47	0.60	38	0.44	53	0.55
PER2	2	54	0.63	54	0.40	68	0.59
PER3	1	60	0.68	84	0.15	101	0.047
Pathway-level		653	0.021	670	0.76	842	0.17
Melatonin pathway							
AANAT	17	53	0.59	52	0.85	61	0.91
DDC	7	119	0.89	115	0.58	147	0.74
MTNR1A	4	60	0.18	61	0.86	72	0.30
MTNR1B	11	33	0.92	34	0.87	45	0.96
TPH1	11	20	0.029	22	0.27	27	0.068
TPH2	12	67	0.77	92	0.0064	107	0.013
Pathway-level		352	0.24	376	0.066	459	0.091

P<0.05 in bold. None of gene based or pathway based p values reached Bonferroni corrected significance

Supplementary table 5. Gene- and pathway-based p-values for lung and ovarian cancers in GAME-ON

Gene	Chr	Lung cancer (12537 cases, 17285 controls)		Ovarian cancer (4369 cases, 9123 controls)	
		N.SNP*	P-value	N.SNP*	P-value
Circadian rhythm pathway					
ARNTL	11	78	0.18	80	0.58
CK1E	22	47	0.35	48	0.024
CLOCK	4	24	0.19	24	0.20
CRY1	12	33	0.40	35	0.29
CRY2	11	18	0.52	20	0.13
NPAS2	2	165	0.56	167	0.046
PER1	17	29	0.35	30	0.87
PER2	2	50	0.87	50	0.54
PER3	1	66	0.90	67	0.68
Pathway-level		510	0.71	521	0.14
Melatonin pathway					
AANAT	17	30	0.63	38	0.14
DDC	7	82	0.089	84	0.10
MTNR1A	4	35	0.93	35	0.20
MTNR1B	11	21	0.85	23	0.64
TPH1	11	17	0.23	18	0.21
TPH2	12	58	0.048	65	0.75
Pathway-level		243	0.22	263	0.26

*SNP numbers after the LD pruning, using $r^2 > 0.95$

P<0.05 in bold. None of gene- or pathway-level p-values reached the Bonferroni correction threshold of significance.